```
=> s wound (w) kallikrein
L1            0 WOUND (W) KALLIKREIN

=> s kallikrein
L2        35748 KALLIKREIN

=> s wound(w) dressing
L3         8565 WOUND(W) DRESSING

=> s l2 and l3
L4            4 L2 AND L3

=> d

L4   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2004:965119  CAPLUS
DN   141:401017
TI   Pain-sensitive therapeutic wound dressings
IN   Trotter, Patrick John; Cullen, Breda Mary
PA   Johnson & Johnson Medical Limited, UK
SO   PCT Int. Appl., 21 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 2
     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
PI   WO 2004096302         A1    20041111    WO 2004-GB1774          20040427
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     GB 2401041            A1    20041103    GB 2003-9645            20030428
     EP 1620138            A1    20060201    EP 2004-729670          20040427
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
PRAI GB 2003-9645          A     20030428
     US 2003-526973P       P     20031203
     WO 2004-GB1774        W     20040427
RE.CNT  8     THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d 2-4

L4   ANSWER 2 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2004:923217  CAPLUS
DN   141:400989
TI   Pain-sensitive therapeutic wound dressings containing
     matrix of polymers crosslinked with oligopeptides
IN   Trotter, Patrick John; Cullen, Breda Mary
PA   Johnson & Johnson Medical Limited, UK
SO   Brit. UK Pat. Appl., 19 pp.
     CODEN: BAXXDU
DT   Patent
LA   English
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FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 2401041	A1	20041103	GB 2003-9645	20030428
	WO 2004096302	A1	20041111	WO 2004-GB1774	20040427
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1620138	A1	20060201	EP 2004-729670	20040427
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
PRAI	GB 2003-9645	A	20030428		
	US 2003-526973P	P	20031203		
	WO 2004-GB1774	W	20040427		

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:454018 CAPLUS
DN 139:26648
TI Controlled release therapeutic ***wound dressings***
IN Cullen, Breda Mary; Silcock, Derek; Warrick, Jonathan
PA Johnson & Johnson Medical Limited, UK
SO Brit. UK Pat. Appl., 18 pp.
CODEN: BAXXDU
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 2382775	A1	20030611	GB 2001-29292	20011206
	GB 2382775	B2	20050525		
	WO 2003047643	A1	20030612	WO 2002-GB5522	20021206
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002347354	A1	20030617	AU 2002-347354	20021206
	EP 1463539	A1	20041006	EP 2002-783289	20021206
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	JP 2005511147	T2	20050428	JP 2003-548897	20021206
	US 2005159695	A1	20050721	US 2003-497442	20021206
PRAI	GB 2001-29292	A	20011206		
	WO 2002-GB5522	W	20021206		

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 4 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

AN 2004249155 EMBASE
TI The challenge of improving therapy of surgical intensive care patients.
AU Aasen A.O.
CS Dr. A.O. Aasen, Institute of Surgical Research, Department of Surgery, Rikshospitalet University Hospital, NO-0027 Oslo, Norway. a.o.aasen@klinmed.uio.no
SO Surgical Infections, (2004) Vol. 5, No. 1, pp. 3-7. .
ISSN: 1096-2964 CODEN: SIUNAL
CY United States
DT Journal; Article
FS 004 Microbiology
005 General Pathology and Pathological Anatomy
009 Surgery
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
037 Drug Literature Index
LA English
ED Entered STN: 28 Jun 2004
Last Updated on STN: 28 Jun 2004

=> s kallikrein and polymer
L5 200 KALLIKREIN AND POLYMER

=> s kallikrein and hpma and wound
L6 0 KALLIKREIN AND HPMA AND WOUND

=> s kallikrein and hpma
L7 0 KALLIKREIN AND HPMA

=> s hpma(w) ((crosslinked) or (cross (w) linked) or (cross (w) linking))
L8 0 HPMA(W) ((CROSSLINKED) OR (CROSS (W) LINKED) OR (CROSS (W) LINKING))

=> s bradykinin and wound (w) dressing
L9 3 BRADYKININ AND WOUND (W) DRESSING

=> d 1-3

L9 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:439718 CAPLUS
DN 144:475019
TI Bioactive ***wound dressings*** and implantable devices and methods of use
IN Carpenter, Kenneth W.; Turnell, William G.; Defife, Kristin M.; Grako, Kathryn A.
PA Medivas, LLC, USA
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006050091	A2	20060511	WO 2005-US38925	20051027

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,

CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2004-623446P P 20041028

L9 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1262694 CAPLUS
DN 144:27557
TI Wound healing polymer compositions
IN Carpenter, Kenneth W.; Zhang, Huashi; McCarthy, Brendan J.; Szinai, Istvan; Turnell, William G.; Gopalan, Sindhu M.
PA Medivas, LLC, USA
SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005112587	A2	20051201	WO 2005-US16678	20050512

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2004-570668P P 20040512
US 2004-605381P P 20040827

L9 ANSWER 3 OF 3 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
AN 2004249155 EMBASE
TI The challenge of improving therapy of surgical intensive care patients.
AU Aasen A.O.
CS Dr. A.O. Aasen, Institute of Surgical Research, Department of Surgery, Rikshospitalet University Hospital, NO-0027 Oslo, Norway. a.o.aasen@klinmed.uio.no
SO Surgical Infections, (2004) Vol. 5, No. 1, pp. 3-7.
ISSN: 1096-2964 CODEN: SIUNAL
CY United States
DT Journal; Article
FS 004 Microbiology
005 General Pathology and Pathological Anatomy
009 Surgery
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
037 Drug Literature Index
LA English
ED Entered STN: 28 Jun 2004
Last Updated on STN: 28 Jun 2004

=> s wound (w) dressing and therapeutic (w) agent
L10 57 WOUND (W) DRESSING AND THERAPEUTIC (W) AGENT

=> s wound (w) dressing and absorbent
L11 398 WOUND (W) DRESSING AND ABSORBENT

```
=> s l11 and l10
L12          6 L11 AND L10

=> d 1-6

L12  ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2004:965119  CAPLUS
DN   141:401017
TI   Pain-sensitive therapeutic wound dressings
IN   Trotter, Patrick John; Cullen, Breda Mary
PA   Johnson & Johnson Medical Limited, UK
SO   PCT Int. Appl., 21 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 2
     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
PI   WO 2004096302         A1    20041111    WO 2004-GB1774           20040427
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     GB 2401041           A1    20041103    GB 2003-9645             20030428
     EP 1620138           A1    20060201    EP 2004-729670           20040427
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
PRAI GB 2003-9645          A     20030428
     US 2003-526973P       P     20031203
     WO 2004-GB1774        W     20040427
RE.CNT  8     THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12  ANSWER 2 OF 6  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2004:282763  CAPLUS
DN   140:309375
TI   Wound dressing with controlled release of
     therapeutic agent
IN   Trotter, Patrick John; Silcock, Derek
PA   Johnson & Johnson Medical Limited, UK
SO   Brit. UK Pat. Appl., 24 pp.
     CODEN: BAXXDU
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
PI   GB 2393656           A1     20040407    GB 2002-22722            20021001
     GB 2393656           B2     20051116
     WO 2004030711        A1     20040415    WO 2003-GB4250           20031001
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
             LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
             OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	AU 2003299184	A1	20040423	AU 2003-299184	20031001
	EP 1545637	A1	20050629	EP 2003-756550	20031001
	EP 1545637	B1	20060802		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	AT 334705	E	20060815	AT 2003-756550	20031001
PRAI	GB 2002-22722	A	20021001		
	WO 2003-GB4250	W	20031001		

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:252378 CAPLUS
DN 140:259064
TI ***Wound dressings*** with materials for the controlled release of ***therapeutic agents*** and use for the treatment of wound infection
IN Watt, Paul
PA Johnson & Johnson Medical Limited, UK
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004024196	A1	20040325	WO 2003-GB3886	20030910
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	GB 2392836	A1	20040317	GB 2002-21064	20020911
	GB 2392836	B2	20050525		
	AU 2003263332	A1	20040430	AU 2003-263332	20030910
PRAI	GB 2002-21064	A	20020911		
	US 2003-472126P	P	20030519		
	WO 2003-GB3886	W	20030910		

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:213312 CAPLUS
DN 140:259059
TI ***Wound dressings*** for the controlled release of ***therapeutic agents*** into wounds and treatment of wound infection
IN Watt, Paul William
PA Johnson & Johnson Medical Limited, UK
SO Brit. UK Pat. Appl., 18 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI GB 2392836 A1 20040317 GB 2002-21064 20020911
GB 2392836 B2 20050525
WO 2004024196 A1 20040325 WO 2003-GB3886 20030910
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2003263332 A1 20040430 AU 2003-263332 20030910
PRAI GB 2002-21064 A 20020911
US 2003-472126P P 20030519
WO 2003-GB3886 W 20030910
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:454018 CAPLUS
DN 139:26648
TI Controlled release therapeutic ***wound dressings***
IN Cullen, Breda Mary; Silcock, Derek; Warrick, Jonathan
PA Johnson & Johnson Medical Limited, UK
SO Brit. UK Pat. Appl., 18 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2382775	A1	20030611	GB 2001-29292	20011206
GB 2382775	B2	20050525		
WO 2003047643	A1	20030612	WO 2002-GB5522	20021206
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002347354	A1	20030617	AU 2002-347354	20021206
EP 1463539	A1	20041006	EP 2002-783289	20021206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005511147	T2	20050428	JP 2003-548897	20021206
US 2005159695	A1	20050721	US 2003-497442	20021206
PRAI GB 2001-29292	A	20011206		
WO 2002-GB5522	W	20021206		

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:489268 CAPLUS
DN 135:82054
TI Fibers providing controlled active agent delivery
IN Di Luccio, Robert Cosmo; Akin, Frank Jerrel
PA Kimberly-Clark Worldwide, Inc., USA
SO PCT Int. Appl., 24 pp.

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     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.            KIND   DATE        APPLICATION NO.          DATE
     ---------------       ----   --------    --------------------     --------
PI   WO 2001047567          A2    20010705    WO 2000-US33184          20001208
     WO 2001047567          A3    20011206
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
             ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     GB 2373477             A1    20020925    GB 2002-16125            20001208
     GB 2373477             B2    20040225
     DE 10085395            T     20021205    DE 2000-10085395         20001208
     BR 2000016788          A     20030225    BR 2000-16788            20001208
     US 2004082239          A1    20040429    US 2003-600301           20030620
PRAI US 1999-173193P        P     19991227
     US 2000-716665         A     20001120
     WO 2000-US33184        W     20001208


=> s wound (w) dressing and therapeutic (w) agent and absorbent
L13          6 WOUND (W) DRESSING AND THERAPEUTIC (W) AGENT AND ABSORBENT

=> s bradykinin and wound (w) dressing and therapeutic (w) agent
L14          0 BRADYKININ AND WOUND (W) DRESSING AND THERAPEUTIC (W) AGENT

=> s bradykinin and wound and therapeutic (w) agent
L15          5 BRADYKININ AND WOUND AND THERAPEUTIC (W) AGENT

=> d 1-5

L15  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   1999:743354  CAPLUS
DN   132:102894
TI   Neuropeptides: Their significance in the skin
AU   Wallengren, Joanna
CS   Dept. of Dermatology and Venereology, Lund University Hospital, Lund,
     SE-221 85, Swed.
SO   Drug News & Perspectives (1999), 12(7), 401-411
     CODEN: DNPEED; ISSN: 0214-0934
PB   Prous Science
DT   Journal; General Review
LA   English
RE.CNT  105   THERE ARE 105 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15  ANSWER 2 OF 5  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   1992:547813  CAPLUS
DN   117:147813
TI   Uptake of polyamines by human endothelial cells.  Characterization and
     lack of effect of agonists of endothelial function
AU   Morgan, David M. L.
CS   Vasc. Biol. Res. Cent., King's Coll., London, W8 7AH, UK
SO   Biochemical Journal (1992), 286(2), 413-17
     CODEN: BIJOAK; ISSN: 0306-3275
DT   Journal
LA   English
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L15 ANSWER 3 OF 5 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
AN 92281542 EMBASE
DN 1992281542
TI Uptake of polyamines by human endothelial cells: Characterization and lack of effect of agonists of endothelial function.
AU Morgan D.M.L.
CS Vascular Biology Research Centre, Biomedical Sciences Division, King's College London, Campden Hill Road,London W8 7AH, United Kingdom
SO Biochemical Journal, (1992) Vol. 286, No. 2, pp. 413-417. .
ISSN: 0264-6021 CODEN: BIJOAK
CY United Kingdom
DT Journal; Article
FS 029 Clinical Biochemistry
037 Drug Literature Index
LA English
SL English
ED Entered STN: 11 Oct 1992
Last Updated on STN: 11 Oct 1992

L15 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AN 1992:520740 BIOSIS
DN PREV199294128815; BA94:128815
TI UPTAKE OF POLYAMINES BY HUMAN ENDOTHELIAL CELLS CHARACTERIZATION AND LACK OF EFFECT OF AGONISTS OF ENDOTHELIAL FUNCTION.
AU MORGAN D M L [Reprint author]
CS VASCULAR BIOLOGY RES CENTRE, BIOMEDICAL SCIENCES DIV, KING'S COLL LONDON, CAMPDEN HILL ROAD, LONDON W8 7AH, UK
SO Biochemical Journal, (1992) Vol. 286, No. 2, pp. 413-417.
ISSN: 0264-6021.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 19 Nov 1992
Last Updated on STN: 19 Nov 1992

L15 ANSWER 5 OF 5 MEDLINE on STN
AN 92412011 MEDLINE
DN PubMed ID: 1530574
TI Uptake of polyamines by human endothelial cells. Characterization and lack of effect of agonists of endothelial function.
AU Morgan D M
CS Vascular Biology Research Centre, King's College London, U.K.
SO The Biochemical journal, (1992 Sep 1) Vol. 286 (Pt 2), pp. 413-7.
Journal code: 2984726R. ISSN: 0264-6021.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199210
ED Entered STN: 6 Nov 1992
Last Updated on STN: 29 Jan 1999
Entered Medline: 19 Oct 1992

=> s kallikrein and wound (w) healing
L16 101 KALLIKREIN AND WOUND (W) HEALING

=> d 1-5 abs

L16 ANSWER 1 OF 101 CAPLUS COPYRIGHT 2006 ACS on STN
AB Simultaneous ablation of the two known activators of plasminogen (Plg), urokinase-type (uPA) and tissue-type (tPA), results in a substantial delay

in skin ***wound healing***. However, wound closure and epidermal re-epithelialization are significantly less impaired in uPA;tPA double-deficient mice than in Plg-deficient mice. Skin wounds in uPA;tPA-deficient mice treated with the broad-spectrum matrix metalloproteinase (MMP) inhibitor galardin (N-[(2R)-2-(hydroxamido-carbonylmethyl)-4-methylpentanoyl]-L-tryptophan methylamide) eventually heal, whereas skin wounds in galardin-treated Plg-deficient mice do not heal. Furthermore, plasmin is biochem. detectable in wound exts. from uPA;tPA double-deficient mice. In vivo administration of a plasma ***kallikrein*** (pKal)-selective form of the serine protease inhibitor ecotin exacerbates the healing impairment of uPA;tPA double-deficient wounds to a degree indistinguishable from that observed in Plg-deficient mice, and completely blocks the activity of pKal, but not uPA and tPA in wound exts. These findings demonstrate that an addnl. plasminogen activator provides sufficient plasmin activity to sustain the healing process albeit at decreased speed in the absence of uPA, tPA and galardin-sensitive MMPs and suggest that pKal plays a role in plasmin generation.

L16 ANSWER 2 OF 101 CAPLUS COPYRIGHT 2006 ACS on STN
AB C-terminal amidated human parathyroid hormone analogs PTH 1-32-NH2 and PTH 1-33-NH2 are biol. active and can be used for the treatment of various bone related diseases and conditions. Pharmaceutical compns. are claimed comprising a pharmaceutically effective amount of a C-terminal amidated human parathyroid hormone analog, a pH-lowering agent, an absorption enhancer, a protease inhibitor, and an acid resistant protective vehicle.

L16 ANSWER 3 OF 101 CAPLUS COPYRIGHT 2006 ACS on STN
AB Polynucleotide and polypeptide sequences are identified that are associated with, regulated in, and/or regulate the NF-κB pathway in human THP-1 cell. The identification of such polynucleotides and polypeptides were identified utilizing subtraction library technol., PCR expression profiling, and microarray technol., and verified as being of functional relevance by antisense oligonucleotide methodol. and gene knockout studies. These polypeptides and proteins are an advancement toward discovering and identifying new drug targets for the treatment of NF-κB pathway-related diseases, disorders, and conditions. The invention further relates to compns. and methods for the treatment of diseases or disorders associated with the NF-κB signaling pathway using the sequences of the invention.

L16 ANSWER 4 OF 101 CAPLUS COPYRIGHT 2006 ACS on STN
AB During dermal injury and inflammation the serine proteases ***kallikreins*** cleave endogenous, multifunctional substrates (kininogens) to form bradykinin and kallidin. The actions of kinins are mediated by preferential binding to constitutively expressed kinin-B2 receptors or inducible kinin-B1 receptors. A feature of the kinin-B1 receptors is that they show low levels of expression, but are distinctly upregulated following tissue injury and inflammation. Because recent evidence suggested that kinin-B1 receptors may perform a protective role during inflammation, the authors investigated the specific occurrence of the ***kallikrein***-kinin components in skin biopsies obtained from normal skin, patients undergoing surgery, basalioma, lichenificated atopic eczema, and psoriasis. The tissue was immunolabeled to determine the localization of tissue pro-***kallikrein***, ***kallikrein***, kininogen and kinin receptors. The kinin components were visualized in normal, diseased and traumatized skin, except that no labeling was observed for kininogen in normal skin. Of the 5 types of tissue examined, upregulation of kinin-B1 receptors was observed only in skin biopsies obtained following surgery. In essence, the expression of kinin-B1 receptors did not appear to be enhanced in the other biopsies. Within the multiple steps of the inflammatory cascade in ***wound healing***, these results suggest an important regulatory role for kinin-B1 receptors during the first phase of inflammation following

injury.

L16 ANSWER 5 OF 101 CAPLUS COPYRIGHT 2006 ACS on STN
AB The invention provides a wound dressing comprising a therapeutic agent and a matrix comprising polymers joined by crosslinkages which crosslinkages comprise oligopeptidic sequences which are cleavable by a ***kallikrein*** associated with wound fluid such that the rate of release of the therapeutic agent increases in the presence of elevated ***kallikrein*** levels. For example, the polymer is a homopolymer of N-2-hydroxypropyl methacrylamide, the oligopeptide comprises of sequence of Phe-Arg-Ser-Ser-Arg-Gln, and the therapeutic agent can be antimicrobials, analgesics, anesthetics and ***kallikrein*** inhibitor.

=> d 6-10 abs

L16 ANSWER 6 OF 101 CAPLUS COPYRIGHT 2006 ACS on STN
AB Polynucleotide and polypeptide sequences are identified that are associated with, regulated in, and/or regulate the NF-κB pathway in human THP-1 cell. The identification of such polynucleotides and polypeptides were identified utilizing subtraction library technol., PCR expression profiling, and microarray technol., and verified as being of functional relevance by antisense oligonucleotide methodol. and gene knockout studies. These polypeptides and proteins are an advancement toward discovering and identifying new drug targets for the treatment of NF-κB pathway-related diseases, disorders, and conditions. The invention further relates to compns. and methods for the treatment of diseases or disorders associated with the NF-κB signaling pathway using the sequences of the invention.

L16 ANSWER 7 OF 101 CAPLUS COPYRIGHT 2006 ACS on STN
AB A method and solution for perioperatively inhibiting tumor cell adhesion and a variety of pain and inflammation processes at wounds from general surgical procedures including oral/dental procedures is described. The solution preferably includes at least one antitumor cell adhesion agent and multiple pain and inflammation inhibitory agents at dilute concentration in a physiol. carrier, such as saline or lactated Ringer's solution The solution is applied by continuous irrigation of a wound during a surgical procedure for preemptive inhibition of pain and while avoiding undesirable side effects associated with oral, i.m., s.c. or i.v. application of larger doses of the agents. One preferred solution to inhibit tumor cell adhesion, pain and inflammation includes at least one anti-tumor cell adhesion agent, a serotonin2 antagonist, a serotonin+iquest;3 antagonist, a histamine antagonist, a serotonin agonist, a cyclooxygenase inhibitor, a neurokininl antagonist, a neurokinin2 antagonist, a purinoceptor antagonist, an ATP-sensitive potassium channel opener, a calcium channel antagonist, a bradykininl antagonist, a bradykinin2 antagonist and a μ-opioid agonist. Solns. for anat. joint irrigation during arthroscopy included such compds. as amitriptyline, metoclopramide, sumatriptan, and HOE 140.

L16 ANSWER 8 OF 101 CAPLUS COPYRIGHT 2006 ACS on STN
AB Macrophage migration inhibitory factor (MIF), a proinflammatory cytokine, has been shown to play a role in ***wound-healing*** processes. In this study, the authors investigated whether protease-activated receptor (PAR)-1 and PAR-2 mediated MIF expression in human endothelial cells. Thrombin, factor Xa (FXa), and trypsin induced MIF expression in human dermal microvascular endothelial cells and human umbilical vein endothelial cells, but other proteases, including ***kallikrein*** and urokinase, failed to do so. Thrombin-induced MIF mRNA expression was significantly reduced by the thrombin-specific inhibitor hirudin. Thrombin receptor activation peptide-6, a synthetic PAR-1 peptide, induced MIF mRNA expression, suggesting that PAR-1 mediates MIF expression in response to thrombin. The effects of FXa were blocked

by antithrombin III, but not by hirudin, indicating that FXa might enhance MIF production directly rather than via thrombin stimulation. The synthetic PAR-2 peptide SLIGRL-NH2 induced MIF mRNA expression, showing that PAR-2 mediated MIF expression in response to FXa. Concerning the signal transduction, a mitogen-activated protein kinase kinase inhibitor (PD98089) and a nuclear factor (NF)-κB inhibitor (SN50) suppressed the up-regulation of MIF mRNA in response to thrombin, FXa, and PAR-2 agonist stimulation, whereas a p38 inhibitor (SB203580) had little effect. These facts indicate that up-regulation of MIF by thrombin or FXa is regulated by p44/p42 mitogen-activated protein kinase-dependent pathways and NF-κB-dependent pathways. Moreover, the authors found that PAR-1 and PAR-2 mRNA expression in endothelial cells was enhanced by MIF. Furthermore, the authors examined the inflammatory response induced by PAR-1 and PAR-2 agonists injected into the mouse footpad. As shown by footpad thickness, an indicator of inflammation, MIF-deficient mice (C57BL/6) were much less sensitive to either PAR-1 or PAR-2 agonists than wild-type mice. Taken together, these results suggest that MIF contributes to the inflammatory phase of the ***wound healing*** process in concert with thrombin and FXa via PAR-1 and PAR-2.

L16 ANSWER 9 OF 101 CAPLUS COPYRIGHT 2006 ACS on STN

AB Connective tissue growth factor (CTGF) stimulates cell proliferation, migration, adhesion and extracellular matrix production, and functions in processes such as development, differentiation, angiogenesis, implantation, ***wound healing*** and fibrosis. CTGF is a 38 kDa protein that comprises four discrete structural modules (modules 1-4) but is susceptible to limited proteolysis in utero yielding bioactive isoforms that comprise either modules 3 and 4 (16-20 kDa) or module 4 (10 kDa). Here we report the development of a stable cell line, termed DB1, that was generated by transfecting cDNA encoding full-length human CTGF into Chinese hamster ovary cells that were mutant for heparin sulfate and chondroitin sulfate. DB1 cells produced 38 kDa CTGF and low mol. mass CTGFs that had N-termini between modules 2 and 3 at Ala181 (20 kDa), Leu184 (18 kDa) or Ala197 (16 kDa) or between modules 3 and 4 at Gly253 (10 kDa). CTGF was exported from DB1 cells as early as 5 min after synthesis and all isoforms were readily purified from conditioned medium by sequential steps of heparin affinity, cation exchange, and reverse-phase chromatog. The 38 kDa CTGF was faithfully glycosylated and underwent limited proteolysis in the presence of thrombin, ***kallikrein*** or uterine fluids, the last of which was antagonized by anti-thrombin III. All CTGF isoforms promoted cell adhesion, mitosis and epithelial transdifferentiation in vitro as well as s.c. fibrosis in vivo. The establishment of this recombinant expression system allows for mass-scale production of all previously reported uterine CTGF isoforms, demonstrates that module 4 contains functional domains involved in a broad range of biol. activities, and will facilitate studies of CTGF processing in vitro.

L16 ANSWER 10 OF 101 CAPLUS COPYRIGHT 2006 ACS on STN

AB Larvae of the greenbottle fly Lucilia sericata are used routinely for the clin. treatment of difficult necrotic and infected wounds. Degradation by proteinases contained in larval excretory/secretory (ES) products is thought to contribute to wound debridement by removal of dead tissue. However, proteinase activity may also affect host tissue remodeling processes. The aim of this study was to identify proteolytic enzymes derived from L. sericata ES products with activities against fibrin and extracellular matrix (ECM) components. Larval proteinase activities were assayed in vitro using class-specific substrates and inhibitors. Their action against fibrin and ECM components was examined using SDS-PAGE. Three classes of proteolytic enzyme were detected in the secretions using fluorescein isothiocyanate-labeled casein as a model substrate. The predominant activity belonged to serine proteinases (pH optima 8-9) of two different subclasses (trypsin-like and chymotrypsin-like), with a weaker aspartyl proteinase (pH 5) and a metalloproteinase (pH 9) with

exopeptidase characteristics also present. Using skin-relevant ECM components as substrates L. sericata ES products solubilized fibrin clots and degraded fibronectin, laminin and acid-solubilized collagen types I and III. Hydrolysis of ECM macromols. was inhibited by preincubating ES products with phenylmethylsulfonyl fluoride but not 4-amidinophenylmethylsulfonyl fluoride, indicating that degradation was due to the 'chymotrypsin-like' serine proteinase. These data suggest that a combination of L. sericata ES proteinases involving chymotrypsin-like and trypsin-like activities could potentially influence ***wound healing*** events when maggots are introduced into necrotic and infected wounds, with the chymotrypsin-like activity involved in the remodeling of ECM components.

=> d 60-70 abs

L16 ANSWER 60 OF 101 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

L16 ANSWER 61 OF 101 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AB Macrophage migration inhibitory factor (MIF), a proinflammatory cytokine, has been shown to play a role in ***wound-healing*** processes. In this study, we investigated whether protease-activated receptor (PAR)-1 and PAR-2 mediated MIF expression in human endothelial cells. Thrombin, factor Xa (FXa), and trypsin induced MIF expression in human dermal microvascular endothelial cells and human umbilical vein endothelial cells, but other proteases, including ***kallikrein*** and urokinase, failed to do so. Thrombin-induced MIF mRNA expression was significantly reduced by the thrombin-specific inhibitor hirudin. Thrombin receptor activation peptide-6, a synthetic PAR-1 peptide, induced MIF mRNA expression, suggesting that PAR-1 mediates MIF expression in response to thrombin. The effects of FXa were blocked by antithrombin III, but not by hirudin, indicating that FXa might enhance MIF production directly rather than via thrombin stimulation. The synthetic PAR-2 peptide SLIGRL-NH2 induced MIF mRNA expression, showing that PAR-2 mediated MIF expression in response to FXa. Concerning the signal transduction, a mitogen-activated protein kinase kinase inhibitor (PD98089) and a nuclear factor (NF)-kappaB inhibitor (SN50) suppressed the up-regulation of MIF mRNA in response to thrombin, FXa, and PAR-2 agonist stimulation, whereas a p38 inhibitor (SB203580) had little effect. These facts indicate that up-regulation of MIF by thrombin or FXa is regulated by p44/p42 mitogen-activated protein kinase-dependent pathways and NF-kappaB-dependent pathways. Moreover, we found that PAR-1 and PAR-2 mRNA expression in endothelial cells was enhanced by MIF. Furthermore, we examined the inflammatory response induced by PAR-1 and PAR-2 agonists injected into the mouse footpad. As shown by footpad thickness, an indicator of inflammation, MIF-deficient mice (C57BL/6) were much less sensitive to either PAR-1 or PAR-2 agonists than wild-type mice. Taken together, these results suggest that MIF contributes to the inflammatory phase of the ***wound healing*** process in concert with thrombin and FXa via PAR-1 and PAR-2.

L16 ANSWER 62 OF 101 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AB Protease activities are both temporally and spatially regulated, with identical proteases often involved in different processes depending on time and location. Plasma ***kallikrein*** (Pkal) for example releases bradykinin and, as we recently showed, serves as a plasminogen activator in adipocyte differentiation during mammary gland involution. To dissect such a specialized protease network there is a need for versatile proteomics tools that can function in parallel with genetic models. Accordingly, we developed libraries of protein inhibitors to serine proteases and showed their initial efficacy with Pkal. Starting from the ecotin scaffold, a macromolecular inhibitor of serine proteases with a trypsin 3-D fold, we modified simultaneously all four surface loops that form the binding interface with Pkal by targeted mutagenesis. Phage-display selection yielded a Pkal inhibitor with an inhibition constant (Ki) of 150 pM, while inhibition constants for related proteases were four orders of magnitude larger. This inhibition profile is explained by a cooperative effect between mutations in the different surface loops of ecotin. Treatment of wild-type and gene-deficient mice with this inhibitor during adipocyte differentiation and ***wound healing*** is elucidating the multiple physiological roles of Pkal.A.S. was supported by the Netherlands Organization for Scientific Research.

L16 ANSWER 63 OF 101 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on

STN

AB Connective tissue growth factor (CTGF) stimulates cell proliferation, migration, adhesion and extracellular matrix production, and functions in processes such as development, differentiation, angiogenesis, implantation, ***wound healing*** and fibrosis. CTGF is a 38 kDa protein that comprises four discrete structural modules (modules 1-4) but is susceptible to limited proteolysis in utero yielding bioactive isoforms that comprise either modules 3 and 4 (16-20 kDa) or module 4 (10 kDa). Here we report the development of a stable cell line, termed DB1, that was generated by transfecting cDNA encoding full-length human CTGF into Chinese hamster ovary cells that were mutant for heparin sulphate and chondroitin sulphate. DB1 cells produced 38 kDa CTGF and low molecular mass CTGFs that had N-termini between modules 2 and 3 at Ala181 (20 kDa), Leu184 (18 kDa) or Ala197 (16 kDa) or between modules 3 and 4 at Gly253 (10 kDa). CTGF was exported from DB1 cells as early as 5 min after synthesis and all isoforms were readily purified from conditioned medium by sequential steps of heparin affinity, cation exchange, and reverse-phase chromatography. The 38 kDa CTGF was faithfully glycosylated and underwent limited proteolysis in the presence of thrombin, ***kallikrein*** or uterine fluids, the last of which was antagonized by anti-thrombin III. All CTGF isoforms promoted cell adhesion, mitosis and epithelial transdifferentiation in vitro as well as subcutaneous fibrosis in vivo. The establishment of this recombinant expression system allows for mass-scale production of all previously reported uterine CTGF isoforms, demonstrates that module 4 contains functional domains involved in a broad range of biological activities, and will facilitate studies of CTGF processing in vitro.

L16 ANSWER 64 OF 101 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

L16 ANSWER 65 OF 101 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AB Angiogenesis is the sprouting of new capillary blood vessels from pre-existing ones. The kinin family of vasoactive peptides, formed by the serine protease tissue ***kallikrein*** from its endogenous multifunctional protein substrate kininogen, is believed to regulate the angiogenic process. The aim of this study was to determine the expression of tissue ***kallikrein*** and kinin receptors in an in vitro model of angiogenesis. Microvascular endothelial cells from the bovine mature and regressing corpus luteum were used only if they reacted with known endothelial cell markers. At first the cultured endothelial cells began sprouting, and within four weeks formed three-dimensional, capillary-like structures. Immunolabelling for tissue prokallikrein and the mature enzyme was intense in the angiogenic endothelial cells derived from mature corpora lutea. Immunoreactivity was lower in non-angiogenic endothelial cells and least in angiogenic endothelial cultures of the regressing corpus luteum. Additionally, using specific antisense DIG-labelled probes, tissue ***kallikrein*** mRNA was demonstrated in cells of the angiogenic phenotype. Immunolabelled kinin B2 receptors, but not kinin B1 receptors, were visualised on angiogenic endothelial cells. Our results suggest an important regulatory role for kinins in the multiple steps of the angiogenic cascade that may occur in ***wound healing*** and cancer cell growth.

L16 ANSWER 66 OF 101 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AB The serine proteinase plasmin is, together with tissue-type plasminogen activator (tPA) and urokinase-type plasminogen activator (uPA), involved in the dissolution of blood clots in a fibrin-dependent manner. Moreover, plasmin plays a key role in a variety of other activation cascades such as the activation of metalloproteinases, and has also been implicated in ***wound healing***, pathogen invasion, cancer invasion and metastasis. The leech-derived (Hirudo medicinalis) antistasin-type

inhibitor bdellastasin represents a specific inhibitor of trypsin and plasmin and thus offers a unique opportunity to evaluate the concept of plasmin inhibition. The complexes formed between bdellastasin and bovine as well as porcine beta-trypsin have been crystallised in a monoclinic and a tetragonal crystal form, containing six molecules and one molecule per asymmetric unit, respectively. Both structures have been solved and refined to 3.3 ANG and 2.8 ANG resolution. Bdellastasin turns out to have an antistasin-like fold exhibiting a bis-domainal structure like the tissue ***kallikrein*** inhibitor hirustasin. The interaction between bdellastasin and trypsin is restricted to the C-terminal subdomain of bdellastasin, particularly to its primary binding loop, comprising residues Asp30-Glu38. The reactive site of bdellastasin differs from other antistasin-type inhibitors of trypsin-like proteinases, exhibiting a lysine residue instead of an arginine residue at P1. A model of the bdellastasin-microplasmin complex has been created based on the X-ray structures. Our modelling studies indicate that both trypsin and microplasmin recognise bdellastasin by interactions which are characteristic for canonically binding proteinase inhibitors. On the basis of our three-dimensional structures, and in comparison with the tissue-***kallikrein***-bound and free hirustasin and the antistasin structures, we postulate that the binding of the inhibitors toward trypsin and plasmin is accompanied by a switch of the primary binding loop segment P5-P3. Moreover, in the factor Xa inhibitor antistasin, the core of the molecule would prevent an equivalent rotation of the P3 residue, making exosite interactions of antistasin with factor Xa imperative. Furthermore, Arg32 of antistasin would clash with Arg175 of plasmin, thus impairing a favourable antistasin-plasmin interaction and explaining its specificity.

L16 ANSWER 67 OF 101 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AB Promacrophage-stimulating protein (MSP) is an 80-kDa protein that acquires biological activity after cleavage at an Arg-Val bond to a disulfide-linked alpha-beta heterodimer by serine proteases of the intrinsic coagulation cascade. These proteases, which include serum ***kallikrein***, factor XIIa and factor XIa, are members of the trypsin family of serine proteases. We now report that two other members of the family, nerve growth factor-gamma (NGF-gamma) and epidermal growth factor-binding protein (EGF-BP), cleave and activate pro-MSP to the disulfide-linked alpha-beta heterodimer. Cleavage of 1.5 nM proMSP by 1 nM NGF-gamma or EGF-BP at 37 degree C was almost complete within 30 min. These concentrations of enzyme are about 2 orders of magnitude less than is required for cleavage by serum ***kallikrein*** or factor XIIa. Cleavage of pro-MSP to MSP was associated with a conformational change in the protein, because the cleaved product, but not pro-MSP, was detected by a sandwich enzyme-linked immunoassay. Cleavage caused the appearance of biological activity, as measured by chemotactic activity of MSP for resident peritoneal macrophages, by MSP-induced macrophage shape change, and by stimulation of macrophage ingestion of C3bi-coated erythrocytes. These findings suggest the possibility of cooperative interactions between NGF-gamma or EGF-BP and pro-MSP in inflammation and wound heating.

L16 ANSWER 68 OF 101 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AB The study of vascular cell function and the interactions of endothelial cells (EC), smooth muscle cells (SMC), and monocyte-derived macrophages has expanded greatly during the past 20 years, and the resultant information has reformed our views on the genesis of atherosclerotic plaque. The concept of an activated or injured endothelium that exhibits properties distinct from healthy adult endothelium is now well accepted. Activated EC may exhibit proatherogenic behavior, including increased leukocyte adhesivity, procoagulant activity, and SMC mitogen production. Thrombin, a coagulation-system protease, may serve as a physiologic activator of EC. Thrombin at sites of vascular injury may stimulate

diverse functions, including increased expression of monocyte adhesion proteins and platelet-derived growth factor (PDGF). The monocyte-derived macrophage has been implicated as a participant in several aspects of atherosclerotic plaque development. The attachment of monocytes to EC is the initial event in the interaction of these cells with the vessel wall. Distinctly focal adhesion of monocytes to EC of large vessels is one of the earliest documented events in experimentally induced atherosclerosis and, thus, regulation of this process may be critical to the development of the disease. Intimal proliferation of SMC is another hallmark of the atherosclerotic lesion. Platelet-derived growth factor is both a chemoattractant and mitogen for SMC. Therefore, if EC secrete PDGF abluminally, both the migration of SMC into the intima and subsequent proliferation will be stimulated. Immunocytochemistry and in situ hybridization have verified that vascular EC express PDGF mRNA and protein in vivo under certain conditions. The intracellular pathways employed by thrombin to stimulate PDGF production by EC are becoming defined, and differences have been found in the signals employed in this process upsilon induced leukocyte adhesion. Therefore, under specific environmental conditions, thrombin may induce both PDGF and monocyte adhesion proteins whereas, in other situations, only one of the two responses is induced. Thus, specific paracrine functions of the EC may be activated temporally to catalyze such processes as ***wound-healing***, inflammation, vascular restenosis, and atherosclerosis. cholesterol, and high apolipoprotein (apo) B. Deoxyribonucleic acid (DNA) markers of lipid abnormalities or hypertension have included LDL receptor defects, lipoprotein lipase deficiency, high Lp(a), familial defective apo B, decreased quantitative levels of apo B, apo E phenotype, angiotensinogen, and 'glucocorticoid remediable aldosteronism (GRA) hypertension.' Also tested in Utah studies, but not found to be DNA markers for hypertension, were the genetic loci for the structural genes for renin and angiotensin-converting enzyme, and the sodium antiport system. In addition, important gene-gene interactions (LDL receptor with apo E2) and gene-environment interactions (***kallikrein*** with potassium intake) were found. Identification of specific sets of causal factors in many subjects with hypertension and dyslipidemia will soon be possible. Of special interest is the intersection in some families of both lipid abnormalities and hypertension involving some of these genetic and environmental factors and producing an especially high risk of early CAD.

L16 ANSWER 69 OF 101 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AB We evaluated the effect of fibronectin (an adhesive protein) and aprotinin (a protease inhibitor) as single or combined topical therapies for primary healing and prevention of recurrent corneal epithelial defects in the rabbit keratectomy wound model. The biological activity of the prepared solutions of rabbit plasma fibronectin (0.6 g/L) was suggested by in vitro assays of rabbit corneal epithelial cell adhesion and gelatin-binding affinity. In the first experiment, we compared fibronectin, albumin (a control nonadhesive protein), and saline. In the second and third experiments, fibronectin supplemented with aprotinin, aprotinin alone, and saline were compared; aprotinin was used at concentrations of 40 and 1000 ***kallikrein*** inactivating units (KIU) per milliliter. Our results suggest that topical fibronectin, 0.6 g/L, as well as aprotinin at 40- and 1000-KIU/mL concentrations, given alone or in combination, neither promote corneal epithelial ***wound healing*** nor prevent recurrent corneal epithelial defects in rabbit keratectomy wounds.

L16 ANSWER 70 OF 101 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN